

processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized. The mammalian protease enzymes play important roles in many different biological processes including, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

In light of the important physiological roles played by protease enzymes, efforts are currently being undertaken by both industry and academia to identify new, native protease homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of novel polypeptides having homology to various protease enzymes, designated herein as PRO1057 polypeptides.

45. PRO1071

Thrombospondin-1 is a trimeric high molecular weight glycoprotein that is released from platelet alpha-granules in response to thrombin stimulation and that is also a transient component of the extracellular matrix in developing and repairing tissues (Adams, Int. J. Biochem. Cell Biol. 29:861-865 (1997) and Qian et al., Proc. Soc. Exp. Biol. Med. 212:199-207 (1996)). A variety of factors regulate thrombospondin expression and the protein is degraded by both extracellular and intracellular routes. Thrombospondin-1 functions as a cell adhesion molecule and also modulates cell movement, cell proliferation, neurite outgrowth and angiogenesis. As such, there is substantial interest in identifying novel polypeptides having homology to thrombospondin. We herein describe the identification and characterization of a novel polypeptide having homology to thrombospondin, designated herein as PRO1071.

46. PRO1072

Studies have reported that the redox state of the cell is an important determinant of the fate of the cell. Furthermore, reactive oxygen species have been reported to be cytotoxic, causing inflammatory disease, including tissue necrosis, organ failure, atherosclerosis, infertility, birth defects, premature aging, mutations and malignancy. Thus, the control of oxidation and reduction is important for a number of reasons, including the control and prevention of strokes, heart attacks, oxidative stress, hypertension and may be associated with the development of malignancies. The levels of antioxidant enzymes, such as reductases, which catalyze the conversion of reactive oxygen species to water have been shown to be low in cancer cells. In particular, malignant prostate epithelium may have lowered expression of such antioxidant enzymes [Baker et al., Prostate 32(4):229-233 (1997)]. In this regard, reductases, are of interest. In addition, the transcription factors, NF-kappa B and AP-1, are known to be regulated by redox state and to affect the expression of a large variety of genes thought to be involved in the pathogenesis of AIDS, cancer, atherosclerosis and diabetic complications. Publications further describing this subject matter include Engman et al., Anticancer Res. (Greece), 17:4599-4605 (1997), Kelsey, et al., Br. J. Cancer, 76(7):852-854 (1997); Friedrich and Weiss, J. Theor. Biol., 187(4):529-40 (1997) and Pieulle, et al., J. Bacteriol., 179(18):5684-92 (1997). Given the physiological

importance of redox reactions *in vivo*, efforts are currently being under taken to identify new, native proteins which are involved in redox reactions. We describe herein the identification of a novel polypeptide which has sequence similarity to reductase enzymes, designated herein as PRO1072.

47. **PRO1075**

Protein disulfide isomerase is an enzymatic protein which is involved in the promotion of correct refolding of proteins through the establishment of correct disulfide bond formation. Protein disulfide isomerase was initially identified based upon its ability to catalyze the renaturation of reduced denatured RNase (Goldberger et al., *J. Biol. Chem.* 239:1406-1410 (1964) and Epstein et al., *Cold Spring Harbor Symp. Quant. Biol.* 28:439-449 (1963)). Protein disulfide isomerase has been shown to be a resident enzyme of the endoplasmic reticulum which is retained in the endoplasmic reticulum via a -KDEL or -HDEL amino acid sequence at its C-terminus.

Given the importance of disulfide bond-forming enzymes and their potential uses in a number of different applications, for example in increasing the yield of correct refolding of recombinantly produced proteins, efforts are currently being undertaken by both industry and academia to identify new, native proteins having homology to protein disulfide isomerase. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel protein disulfide isomerase homologs. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe a novel polypeptide having homology to protein disulfide isomerase, designated herein as PRO1075.

48. **PRO181**

In *Drosophila*, the dorsal-ventral polarity of the egg chamber depends on the localization of the oocyte nucleus and the gurken RNA to the dorsal-anterior corner of the oocyte. Gurken protein presumably acts as a ligand for the *drosophila* EGF receptor (torpedo/DER) expressed in the somatic follicle cells surrounding the oocyte. Cornichon is a gene required in the germline for dorsal-ventral signaling (Roth et al., *Cell* 81:967-978 (1995)). Cornichon, gurken and torpedo also function in an earlier signaling event that establishes posterior follicle cell fates and specifies the anterior-posterior polarity of the egg chamber. Mutations in any or all of these genes prevent the formation of a correctly polarized microtubule cytoskeleton required for proper localization of the anterior and posterior determinants bicoid and oskar and for the asymmetric positioning of the oocyte nucleus. Thus, it is clear that the cornichon gene product plays an important role in early development. We herein describe the identification and characterization of a novel polypeptide having homology to the cornichon protein, designated herein as PRO181.

49. **PRO195**

Efforts are currently being undertaken to identify and characterize novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide, designated herein as PRO195.

50. **PRO865**

Efforts are currently being undertaken to identify and characterize novel secreted proteins. We herein describe the identification and characterization of a novel secreted polypeptide, designated herein as PRO865.

51. **PRO827**

VLA-2 is an cell-surface integrin protein that has been identified and characterized in a number of mammalian organisms, including both mouse and human. VLA-2 has been shown to be a receptor on the surface of cells for echovirus-1 (EV-1) which mediates infection of VLA-2-expressing cells by EV-1 (Zhang et al., Virology 235(2):293-301 (1997) and Bergelson et al., Science 255:1718-1720 (1992)). VLA-2 has also been shown to mediate the interaction of collagen with endothelium during *in vitro* vascular tube formation (Jackson et al., Cell Biol. Int. 18(9):859-867 (1994)). Various other integrin proteins that share various degrees of amino acid sequence homology with VLA-2 have been identified and characterized in a variety of mammalian organism. These integrins have been reported to play important roles in a variety of different physiological functions. Therefore, there is significant interest in identifying novel polypeptides having homology to one or more of the integrin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to VLA-2 integrin protein, designated herein as PRO827.

52. **PRO1114**

Many important cytokine proteins have been identified and characterized and shown to signal through specific cell surface receptor complexes. For example, the class II cytokine receptor family (CRF2) includes the interferon receptors, the interleukin-10 receptor and the tissue factor CRFB4 (Spencer et al., J. Exp. Med. 187:571-578 (1998) and Kotenko et al., EMBO J. 16:5894-5903 (1997)). Thus, the multitude of biological activities exhibited by the various cytokine proteins is absolutely dependent upon the presence of cytokine receptor proteins on the surface of target cells. There is, therefore, a significant interest in identifying and characterizing novel polypeptides having homology to one or more of the cytokine receptor family. We herein describe the identification and characterization of a novel polypeptide having homology to cytokine receptor family-4 proteins, designated herein as PRO1117.

Interferons (IFNs) encompass a large family of secreted proteins occurring in vertebrates. Although they were originally named for their antiviral activity, growing evidence supports a critical role for IFNs in cell growth and differentiation (Jaramillo et al., Cancer Investigation 13(3):327-338 (1995)). IFNs belong to a class of negative growth factors having the ability to inhibit the growth of a wide variety of cells with both normal and transformed phenotypes. IFN therapy has been shown to be beneficial in the treatment of human malignancies such as Kaposi's sarcoma, chronic myelogenous leukemia, non-Hodgkin's lymphoma, and hairy cell leukemia as well as in the treatment of infectious diseases such as hepatitis B (Gamliel et al., Scanning Microscopy 2(1):485-492 (1988), Einhorn et al., Med. Oncol. & Tumor Pharmacother. 10:25-29 (1993), Ringenberg et al., Missouri Medicine 85(1):21-26 (1988), Saracco et al., Journal of Gastroenterology and Hepatology 10:668-673 (1995), Gonzalez-Mateos et al., Hepato-Gastroenterology 42:893-899 (1995) and Malaguarnera et al., Pharmacotherapy 17(5):998-1005 (1997)).

Interferons can be classified into two major groups based upon their primary sequence. Type I